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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/985,756	11/06/2001	Matthew C. Coffey	032775-083	4370

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/985,756	COFFEY, MATTHEW C.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8-30-04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of applicant election without traverse of Group I (claims 1-10) drawn to the method of determining susceptibility of a cell to reovirus.

Claims 11-50, drawn to non-elected inventions, are withdrawn from consideration. Claim 5, drawn to non-elected species, is also withdrawn for consideration.

Claims 1-3 will be examined on the merits. Claims 4 and 6-8 will be examined as they are drawn to the elected species of breast cancer and claims 4, 9-10 will be examined as they are drawn to the elected species of human.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being obvious over Norman et al (J of Clini Invest, Vol. 105, p1035-1038, 2000) in view of Coffey et al (Science Vol 282, p 1332-1334, 1998) and Robinson et al (Curr. Opin. Cell Biol. Vol, 9, p180-186, 1997).

Claim 1 is drawn to a method of determining susceptibility to a cell to reovirus infection by measuring constitutive ras-MAP signaling in said cell, wherein the presence of said constitutive signaling indicates susceptibility to infection by reovirus.

Norman et al teach that constitutive activation of signaling pathways down-stream of ras, such as the mitogen-activated protein kinase (MAPK) is implicated in cellular transformation and progression toward cancer (p 1035, Col 1, ¶ 1). Norman et al also teach that activation of the MAPK pathway has been shown to correlate well with reovirus susceptibility (p 1035, Col 2, ¶ 1).

Coffery et al teach that 80% (20 out of 25) of human cancer cell lines are susceptible to reovirus infection in vitro. Coffey et al teach that there are a strong correlation between infectibility and high basal level of MAP kinase activity (p 1333, Col 3, ¶ 3).

Robinson et al teach that the roles of MAPK pathways in mammalian cell proliferation and differentiation. Robinson et al teach that ERK1 and/or ERK2 (members of MAP kinase family) are activated by mitogens signaling. Functions of ERKs may also contribute to proliferative responses (p182, Col 2, ¶ 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed inventions was made to determine susceptibility to a cell to reovirus infection by measuring constitutive ras-MAP signaling in a cell. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teaching of Norman et al on the correlation of constitutive activation of MAP signaling pathways down-stream of ras with reovirus susceptibility and the teaching of Coffery et al on the susceptibility of human cancer cell lines to reovirus infection in vitro and the teaching of Robinson et al on the contribution of higher ERK1/2 activity to proliferative responses. Therefore, one of skill in the art at the time of invention would conclude that it would be possible to determine the susceptibility of cell to reovirus infection by measuring constitutive ras-MAP signaling in the cells.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Norman et al, Coffey et al and Robinson as applied to claim 1 above, and further in view of Current Protocols in Molecular Biology (unit 14.3, print publication date: Oct 1998).

The embodiments of claim 1 are set forth above. Claim 2 embodies the method of claim 1 wherein the ras-MAP signaling is measured by determining the state of phosphorylation of MAP kinase.

Norman et al, Coffey et al, and Robinson et al teach that constitutive activation of the ras/MAPK pathway contribute to proliferative response in the cancer cells and correlation of the reovirus susceptibility to the cells are set forth above. Norman et al, Coffey et al, and Robinson et al do not teach that the ras-MAP is measured by phosphorylation of MAP kinase. Current Protocols in Molecular Biology teach the method of detection of MAP kinase signaling and protein kinase phosphorylation of MAPK and cascades ras-MAP signaling measured by determining the state of phosphorylation of MAP kinase (p3, ¶ 6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed inventions was made to determine susceptibility of a cells to reovirus infection by measuring constitutive ras-MAP signaling and phosphorylation of MAP kinase in the cells. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teaching of Norman et al, Coffery et al, and Robinson et al on the correlation of constitutive ras-MAP signaling and susceptibility of human cancer cells to reovirus infection in vitro and the teaching of Current Protocols in Molecular Biology on the determination of ras/MAP activity by phosphorylation in the cells. Therefore, one of skill in the art at the time of invention would conclude that it would be possible to determine the susceptibility of cancer cells to reovirus infection by measuring the state of phosphorylation of ras-MAP kinase in those cancer cells.

Claims 1, 2,and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Norman et al, Coffey et al, Robinson et al, and Current Protocols in Molecular Biology as applied to claim 1 and 2 above, and further in view of Wilsbacher et al (J Biol Chem. Vol 272, p16988-16994, 1999).

The embodiments of claim 1 and 2 are set forth above. Claim 3 embodies the method of claim 2 wherein the ras-MAP kinase phosphorylation is determining using an antibody specific for phosphorylated MAP kinase.

Norman et al, Coffey et al, Robinson et al and Current Protocols in Molecular Biology teach that correlation of the constitutive activation of the ras/MAPK and reovirus susceptibility to proliferative or

cancer cells and determination of ras/MAP kinase activity in the cells by phosphorylation. Norman et al, Coffey et al, Robinson et al and Current Protocols in Molecular Biology do not teach that phosphorylation of MAP kinase is measured by antibodies in the method. Wilsbacher et al teach how phosphorylation of MAP kinase were measured and determined by phosphorylated MAP kinase antibody (p 16989, Col 1, ¶ 7 and p 16991, Col 1, ¶ 3).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed inventions was made to determine susceptibility of a cells to reovirus infection by measuring constitutive ras-MAP signaling and phosphorylation of MAP kinase in the cells. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teaching of Norman et al, Coffery et al, and Robinson et al on the correlation of constitutive ras-MAP signaling and susceptibility of human proliferative or cancer cells to reovirus infection in vitro and teaching of Current Protocols in Molecular Biology on the determination of ras/MAP activity by phosphorylation in the cells and by teaching of Wilsbacher et al on the determination of phosphorylation of MAP kinase by an antibody. Therefore, one of skill in the art at the time of invention would conclude that it would be possible to determine the susceptibility of cancer cells to reovirus infection by measuring the state of phosphorylation of ras-MAP kinase by antibodies in those cancer cells.

Claims 1, 4, 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over von Lintig et al (Breast Cancer Research and Treatment, Vol 62, p 51-62, 2000), further in view of Norman et al and Coffey et al, and Robinson et al.

The specific embodiments of claims 1 are set forth above. Claim 4 embodies the method of claim 1 wherein the cell is comprised in a biological sample collected from mammal suspectd of having a proliferative disorder. Claims 6-10 embody the method of claim 4 wherein the proliferative disorder is solid neoplasm and human breast cancer,

von Lintig et al teach ras activation and MAP kinase activity in human breast cancer cell lines . von Lintig et al measured ras activation and MAP kinase activity in human breast tissue and found that samples with high ras activation had high MAP kinase activity and the approximately four-fold higher ras

activation in the cancer group compared to normal breast tissue was reflected in a greater than five-fold increase in MAP kinase activity (p 57, Col 2, ¶ 2). von Lintig et al teach that in the breast cancer cell lines, which contain an activating K-ras, codon 12 mutation, ras activation was high and this cells exhibit similar ras activation as breast cancer tissues (p58, Col 1, ¶ 1 and Col 2, ¶ 1, figure 6 C). von Lintig et al again teach that increase ras activation in these cancer was associated with increased MAP kinase activity (p 59, Col 1, ¶ 2). von Lintig et al do not teach the correlation between susceptibility of reovirus infection and ras/MAP activation in the cancer cells.

Norman et al, Coffey et al, and Robinson et al teach that human reovirus requires an activated ras signaling pathway. Norman et al teach that constitutive activation of signaling pathways down-stream of ras, such as the MAPS is implicated in cellular transformation and progression toward cancer (p 1035, Col 1, ¶ 1). Coffery et al teach that 80% (20 out of 25) of human cancer cell lines are susceptible to reovirus infection in vitro. Coffey et al teach that there are a strong correlation between infectibility and high basal level of MAP kinase activity (p 1333, Col 3, ¶ 3). Robinson et al teach that the roles of MAPK pathways in mammalian cells proliferation and differentiation. Robinson et al teach that functions of ERK may also contribute to proliferative responses (p182, Col 2, ¶ 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed inventions was made to determine susceptibility of breast cancer cells to reovirus infection by measuring constitutive ras-MAP signaling in the cells. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teaching of von Lintig et al on the association of ras activation with increased MAP kinase activity in breast cancer cells and teaching of Norman et al, Coffery et al, and Robinson et al on the contribution of the activation of MAPK pathways to proliferative responses in cells and susceptibility of human cancer cell lines to reovirus infection in vitro. Therefore, one of skill in the art at the time of invention would conclude that it would be possible to determine the susceptibility of human breast cells to reovirus infection by measuring constitutive ras-MAP signaling in those cells.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

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